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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HALVORSON, MARK	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
02/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,873	WARENIUS ET AL.	
	Examiner	Art Unit	
	Mark Halvorson	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 18-28* is/are pending in the application.

4a) Of the above claim(s) *6,9-15 and 18-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on August 16, 2007 has been entered. Submission of the Sequence Listing submitted on July 16, 2008 is acknowledged.

Claims 1-15, 18-28 are pending.

Claim 6, 9-15, 18-28 have been withdrawn.

Claims 1-5, 7 and 8 are under examination.

35 USC § 103(a) rejection withdrawn

The rejection of claims 1, 2 and 7 rejected under 35 U.S.C. 103(a) as being unpatentable over Beach et al (US Patent No: 5,962,316, issued October 5, 1999) in view of Haas et al (Oncogene, 1997, 15:179-192) is withdraw in view of Applicants amendments to claim 1.

35 USC § 103(a) rejection withdrawn

The rejection of claims 1, 2 and 7 rejected under 35 U.S.C. 103(a) as being unpatentable over Beach et al (US Patent No: 5,962,316, issued October 5, 1999) in view of Haas et al (Oncogene, 1997, 15:179-192), further in view of Theryte Limited (WO 99/42821, publication date 26 August 1999) is withdraw in view of Applicants amendments to claim 1.

35 USC § 103(a) rejection withdrawn

The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Beach et al in view of Haas et al as applied to claims 1 and 2, above, and further in view of Ceha et al (Biochem Biophys Res Comm, 1998, 249:550-555), is withdraw in view of Applicants amendments to claim 1.

35 USC § 102(b) rejection maintained

The rejection of claims 1, 2 and 7 under 35 U.S.C. 102(b) as being anticipated by Hybridon (WO 99/27087, published June 3, 1999) is maintained.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 8 is drawn to a method of screening for an agent effective in the treatment of a cancer, comprising selecting a putative agent that is likely to disrupt a function, other than a kinase and a CKI sequestrating activity that is mediated by a critical normal gene product, which functions is required for a successful division and continued cell survival of cancer cells and which functions is not required for the successful division and continued cell survival of control cells; treating a cancer cell sample and a control cell sample with the putative agent and determining the cytotoxic effect and/or growth inhibiting effect of the putative agent on these samples; and identifying an effective agent which is more cytotoxic to, and determining the cytotoxic effect of, and/or the growth of the cancer cell sample than the control sample, wherein the critical normal gene product is human CDK4. The actual function being screened for is not specifically defined in the claims.

Hybridon discloses antisense molecules that bind to the CDK4 gene and inhibit the expression of CDK4 (page 15 line 1 to page 17 line 28) . Hybridon further discloses that other antisense molecules that inhibit CDK4 expression can be identified (page 17

line 30 to page 18 line3). The antisense molecules can be used for treating a mammal afflicted with a tumor associated with the aberrant expression of CDK4 (Abstract). An antisense molecule would suppress expression of the CDK protein and would disrupt the non-kinase function mediated by CDK4.

Applicants argue that Hybridon do not expressly or inherently disclose and therefore, can not anticipate the methods of claim 1, 2 and 7. Applicants argue that Morrissey et al relate to compounds that inhibit expression of CDK4 and thus Hybridon would inhibit all of the functions of CDK4 including its kinase and CKI sequestrating activity. Applicants argue that Hybridon does not expressly or inherently disclose an agent likely to disrupt a function, other than kinase and a CKI sequestrating activity of a critical normal gene product.

Applicants arguments have been considered but are not persuasive. The specification discloses that CDK4 acts to elevate CDK1, p9Ka and possibly CDK2, CDK6 and p27 by a mechanism that is independent of its role in the cell cycle. The claims are drawn to a method for screening for an agent that would disrupt an undisclosed function of CDK4. The undisclosed function is described by what it is not. The function is not a kinase function and is not a CKI sequestering function. The claim recites the limitation “other than a kinase and a CKI sequestrating activity”. Claim 1 has been interpreted such that the function inhibited is distinct from the kinase activity of CDK4 and the CKI sequestrating activity. Claim 1 does not specifically indicate that the agent affecting the undisclosed function of CDK4 does not inhibit the kinase activity and does not involve CKI sequestration. The claim only indicates that the screening method is to identify agents that disrupt an undisclosed function of CDK4. Hybridon does disclose an agent that would disrupt the undisclosed function of CDK4, because Hybridon discloses antisense molecules that bind to the CDK4 gene and inhibit the expression of CDK4, thus disrupting all functions of CDK4.

NEW REJECTIONS:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER.

There is no support in the specification, specifically in paragraphs 60 and 202 for the claim limitation "function other than … a CKI sequestration activity".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (US Patent No: 6,004,939, issued Dec 21, 1999).

The claims are drawn to a method of screening for an agent effective in the treatment of a cancer, comprising selecting a putative agent that is likely to disrupt a function, other than a kinase and a CKI sequestrating activity that is mediated by a critical normal gene product, which functions is required for a successful division and continued cell survival of cancer cells and which functions is not required for the

successful division and continued cell survival of control cells; treating a cancer cell sample and a control cell sample with the putative agent and determining the cytotoxic effect and/or growth inhibiting effect of the putative agent on these samples; and identifying an effective agent which is more cytotoxic to, and determining the cytotoxic effect of, and/or the growth of the cancer cell sample than the control sample, wherein the critical normal gene product is a factor which impedes progress through the cell cycle, an apoptotic factor or a master regulatory gene product, which regulates the levels of other gene products involved in the cell cycle and apoptosis pathways.

Chen et al disclose a method for screening for compounds that inhibit telomerase activity in tumor cells while not affecting normal cells (column 21 line 43 16 to column 25, line 44). Chen et al disclose that certain telomerase inhibitors had differential effects on tumor cells versus normal cells. (Id). Chen et al disclose that the administration of telomerase inhibitors is more detrimental to rapidly growing tumor cells than normal cells. (Id). Chen et al also disclose the therapeutic administration of telomerase inhibitors. (column 28 line 53 to column 31 line 4).

Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Hybridon.

Claim 8 is drawn to a method of screening for an agent effective in the treatment of a cancer, comprising selecting a putative agent that is likely to disrupt a function, other than a kinase and a CKI sequestrating activity that is mediated by a critical normal gene product, which functions is required for a successful division and continued cell survival of cancer cells and which functions is not required for the successful division and continued cell survival of control cells; treating a cancer cell sample and a control cell sample with the putative agent and determining the cytotoxic effect and/or growth inhibiting effect of the putative agent on these samples; and identifying an effective agent which is more cytotoxic to, and determining the cytotoxic effect of, and/or the growth of the cancer cell sample than the control sample, wherein the critical normal gene product is human CDK4, wherein the region of human CDK4 gene product mediating the function required for successful division and controlled cell survival is a

region between amino acids 172-285. The actual function of CDK4 being screened for is not defined.

Hybridon discloses antisense molecules that bind to the CDK4 gene and inhibit the expression of CDK4 (page 15 line 1 to page 17 line 28) . Hybridon further discloses that other antisense molecules that inhibit CDK4 expression can be identified (page 17 line 30 to page 18 line3). The antisense molecules can be used for treating a mammal afflicted with a tumor associated with the aberrant expression of CDK4 (Abstract). An antisense molecule would suppress expression of the CDK protein and would disrupt all functions mediated by CDK4 including non-kinase and CKI sequestrating functions. Thus, the antisense molecule would disrupt the undisclosed function of CDK4 mediated by a region of CDK4 between amino acids 172-285.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hybridon (WO 99/27087, published June 3, 1999) as applied to claims 1, above, and further in view of Theryte Limited (WO 99/42821, publication date 26 August 1999).

Claims 3-5 are drawn to a method of screening for an agent effective in the treatment of a cancer, which method comprises selecting a putative agent that is likely to disrupt a non-kinase function mediated by CDK4 and treating a cancer cell sample and a control cell sample with the putative agent, and determining growth inhibiting effect of the putative agent on these samples and identifying an effective agent as an agent which is more inhibiting to the growth of the cancer cell sample than the control cell sample, wherein the cancer cell sample consists of cancer cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6, wherein the cancer cell sample consists of cells in which the CDK1 and CDK4 gene products are both elevated as compared with control cells, and wherein the step of identifying an effective agent further involves determination of the ratio of the levels of the CDK1 and CDK4 gene products in the cancer cell sample before and after treatment with the putative agent.

Hybridon has been described supra.

Hybridon does not disclose a cancer cell sample that consists of cells in which the CDK1 and CDK4 gene products are both elevated as compared with control cells in which the ratio of the levels of the CDK1 and CDK4 gene products is in the range of 0.6 to 1.6.

Theryte discloses that CDK1 and CDK4 proteins are elevated in cancer cells (Figs. 3 and 4) and that the ration of CDK4 to CDK1 is approximately 1 (Fig 5).

One of ordinary skill in the art would have been motivated to apply Theryte's teaching of the diagnostic value of CDK1 and CDK4 levels in cancer to Hybridon's method of inhibiting CDK4 because Theryte states that the increased levels of CDK1 and CDK4 in cancers may be used in drug screening that might lead to more specifically toxic to cancer tissues (page 3, 3rd paragraph). Thus, it would have been

prima facie obvious to combine Hybridon's method of inhibiting CDK4 with Theryte's finding of elevated levels of CDK4 and CDK1 in cancer.

Summary

Claims 1-5, 7 and 8 stand rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Halvorson, PhD whose telephone number is (571) 272-6539. The examiner can normally be reached on Monday through Friday from 8:30am to 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Mark Halvorson/
Examiner, Art Unit 1642